Application/Control Number 10/748,887 [Docket No.:103832-512NP]

Use of LHRH-antagonists in doses that do not cause castration for the improvement of T-cell mediated immunity

RELATED APPLICATION

This application claims the benefit of priority of U.S. provisional patent application No. 60/309,735, filed August 2, 2001.

FIELD OF THE INVENTION

The field of invention is directed to the use of LHRH-antagonists to modulate male and female human sex hormone levels without reaching a level of castration.

BACKGROUND OF THE INVENTION

In a patent by R.L. Boyd (WO 200062657, AU 200037977) the author claims that disrupting the sex steroid signaling by application of an LHRH-agonist will result in a modification of the T-cell population in subjects with a depressed or abnormal T-cell population. This treatment will have the undesired side-effect of castration of the subject, but the author claims that this castration will be reversible upon cessation of treatment.

This side effect is highly undesirable as it will result in loss or reduction of libido, sexual desire and sexual potency. In men and pre-menopausal women the treatment would also result in the typical symptoms of lowering the sex hormone-level below castration level, e.g. hot flashes, women will additionally be at risk to lose bone minerals, potentially limiting the duration of treatment.

These unwanted effects can be limited by using an LHRH-antagonist in a dose that will not result in castration but will still have the desired effect on the immune system.

SUMMARY OF THE INVENTION

The current invention provides a method of using LHRH-antagonists to modulate male and female human sex hormone levels without reaching a level of castration and avoiding negative side effects. The object has now been achieved in that an LHRH-antagonist is used for the production of a medicament for treating of an individual where the treatment results in a modification of the T-cell population in an individual suffering from a disease that will respond favorable to such a modification suffering from a HIV-infection, cancer, an auto-immune disease, benign prostatic hyperplasia, endometriosis, asthma, arthritis, dermatitis, multiple sclerosis, Jacob Creuzfeldt-disease, or Alzheimer disease. Treatment is also possible to further to enhance the immune response to an antigen, to decrease the host versus graft reaction or to enhance the anti-aging treatment.

The preferred LHRH-antagonist can be cetrorelix, teverelix, iturelix, or abarelix.

Cetrorelix, teverelix, iturelix, and abarelix are all decapeptides with the sequences:

Cetrorelex:	AC-D-Nal(2)-D-pCl-Phe-D-Pal(3)-Ser-Tyr-D-Cit-Leu-Arg-Pro-D-Ala-NH_2
Teverelix:	AC-D-Nal(2)-D-pCl-Phe-D-Pal(3)-Ser-Tyr-D-Hcl-Lys(iPr)-Pro-D-Ala-NH_2
Iturelix:	AC-D-Nal(2)-D-pCl-Phe-D-Pal(3)-Ser-Lys(Nic)-D-Lys(Nic)-Leu-Lys(iPr)-Pro-D-Ala-NH_2
Abrelix:	AC-D-Nal(2)-D-pCl-Phe-D-Pal(3)-Ser-N-Me-Tyr-D-Asn-Leu-Lys(iPr)-Pro-D-Ala-NH_2

Expediently, the medicament can be administered in the following ratio:

Total dose from 5 mg to 120 mg LHRH-antagonist, divided in a period of 1 to 8 weeks and according to needs with repeat of the therapy every 3 to 4 months.

It has been found a preferred embodiment of the therapy with the LHRH-antagonist cetrorelix.

Example 1:

Administer cetrorelix pamoate to a male or female human in a total dose from 30 mg to 120 mg over a period of 1 to 4 weeks, optionally repeating said method of lowering sex hormones.

Example 2:

Administer cetrorelix acetate to a male or female human in a total dose from 5 mg to 80 mg over a period of 1 to 8 weeks, optionally repeating said method of lowering sex hormones.

The preferred therapy with the LHRH-antagonist is based on examining the efficacy of LHRH-antagonists with a patient population of 140 elderly patients (older than 50 years) with benign prostatic hyperplasia and 45 patients with endometriosis in which the immune cell suppression play a role.

In conclusion, the current invention provides a method of using LHRH-antagonists, preferably cetrorelix, to modulate male and female human sex hormone levels without reaching a level of castration and avoiding negative side effects. The total dosage amount to be administered ranges from 5 mg to 120 mg LHRH-antagonist, over a period of 1 to 8 weeks, optionally repeating said method of lowering sex hormones.